149. (New) The array of claim 148 wherein each different substance in a different well is covalently bound to the surface of the solid support.

150. (New) The array of claim 149 wherein each different substance in a different well is covalently bound to the surface of the solid support through a linker.

151. (New) The array of claim 150 wherein the linker is 3-glycidoxypropyltrimethoxysilane.

152. (New) The array of claim 148 wherein each different substance in a different well is non-covalently bound to the surface of the solid support.

153. (New) The array of claim 12 wherein each different substance in a different well is free of binding to the surface of the solid support.

154. (New) The array of claim 12 wherein each different substance in a different well is in solution.

155. (New) The array of claim 12 wherein each well contains reagents for assaying biological activity.

156. (New) The array of claim 12 wherein volumes of the wells are between 1 pl and 5 μl.

157. (New) The array of claim 12 wherein volumes of the wells are between 1 nl and 1 μl.

158. (New) The array of claim 12 wherein volumes of the wells are between 100 nl and 300 nl.

159. (New) The array of claim 12 wherein the bottoms of the wells are square, round, V-shaped or U-shaped.

REMARKS

According to the Office Action mailed October 10, 2002, claims 1-107 are pending in the application and claims 17-92 and 102-105 are withdrawn from consideration.

Claims 17-92 and 102-105 have been cancelled without prejudice as drawn to nonelected inventions in view of the finality of the restriction requirement of April 3, 2002. Applicants reserve the right to prosecute the subject matter of claims 17-92 and 102-105 in one or more related applications. Claims 1, 93 and 100 have been amended to clarify what Applicants consider as the invention. The amendments to claims 1 and 93 are fully supported in the specification, see, *e.g.*, page 5, lines 3-9 and page 25, line 16 to page 26, line 21, and do not represent new subject matter. Support for amended claim 100 can be found, *e.g.*, at page 25, lines 15-26. Claim 93 has been amended to insert "second" before "molecules" merely to distinguish the "other molecules" from those molecules recited in claim 1. New

claims 108-159 have been added to more particularly point out and distinctly claim certain embodiments of the present invention. Support for the new claims can be found in the specification, *e.g.*, as set forth in the chart below.

Claim	Support in the Instant Specification
108, 109	page 26, lines 14-17
110	page 11, lines 19-23;
111	page 26, lines 17-21
112-114	page 25, line 16 to page 26, line 21; page 5, lines 10-17
115	page 25, line 16 to page 26, line 21; page 4, lines 16-21
116-121	page 25, line 16 to page 26, line 21; page 14, lines 26-33;
122-123	page 25, line 16 to page 26, line 21; page 15, lines 7-8;
124	page 25, line 16 to page 26, line 21; page 15, lines 7-15;
125	page 25, line 16 to page 26, line 21; page 15, lines 14-15;
126	page 25, line 16 to page 26, line 21; page 15, lines 7-8;
127	page 25, line 16 to page 26, line 21; page 16, lines 19-21 and 26-28;
128	page 25, line 16 to page 26, line 21; page 16, lines 19-21
129	page 25, lines 22-24
130-132	page 25, line 16 to page 26, line 21; page 13, lines 33-36
133	page 25, line 16 to page 26, line 21; page 13, line 27
134-135	page 11, lines 14-19
136	page 11, lines 19-23
137	page 11, lines 22-25
138-140	page 5, lines 10-17
141	page 4, lines 16-21
142-147	page 14, lines 26-33;
148-149	page 15, lines 7-8;
150	page 15, lines 7-15;
151	page 15, lines 14-15;
152	page 15, lines 7-8;
153	page 16, lines 19-21 and 26-28;
154	page 16, lines 19-21

Claim	Support in the Instant Specification
155	page 25, lines 22-24
156-158	page 13, lines 33-36
159	page 13, line 27

The Rejections Under 35 U.S.C. § 102 Should Be Withdrawn

Claims 1-11 and 106-107 were rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by Wagner et al. (U.S. Patent 6,329,209; "Wagner"). Applicants respectfully assert that Wagner does not anticipate claims 1-11 and 106-107, as amended.

Applicants have amended independent claim 1 to recite the additional limitation that the plurality of proteins or molecules of the array consists of at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, with the same type of biological activity in the genome of an organism.

The standard for an anticipatory reference is set forth in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987): "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See also Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989)(holding that "[t]he identical invention must be shown in as complete detail as is contained in the . . . claim"). Further, a prior art reference must be an *enabling* reference to anticipate. *See* Akzo N.V. v. U.S. Int'l Trade Comm'n, 808 F.2d 1471, 1479 (Fed. Cir. 1986) ("the prior art reference must be enabling, thus placing the allegedly disclosed matter in the possession of the public."). *See also* MPEP § 2121.01; *In re Hoeksema*, 399 F.2d 269 (CCPA 1968) ("In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'.").

Wagner discloses arrays of protein-capture agents which can bind a plurality of proteins. Wagner fails, however, to describe or suggest arrays with at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, with the same type of biological activity of a given organism. In particular, Wagner does not teach how to construct such an array. Wagner discloses arrays of protein-capture agents, that are made by immobilizing protein-capture agents (each capture agent having binding affinity to a protein to be assayed) onto patches on a substrate (see column 3, line 58 to column 4, line

16). Wagner states that the protein-capture agent is typically a biomolecule, and provides antibodies, antigens and receptors as some examples (column 4, lines 54-61). Wagner also teaches that the capture agents can be selected by their binding affinity to proteins. Wagner states that the binding partners of the protein-capture agents of the array can be a wide distribution of different proteins from a single organism (column 12, lines 1-8), and "may optionally all be growth factor receptors, hormone receptors, . . . proteases, kinases, phosphatases . . . ." (column 12, lines 27-32). What is totally lacking from Wagner, however, is how to achieve an array of capture agents that would consist of, or would bind to, at least 50% of all expressed proteins (or molecules comprising the functional domains thereof) of the same type of biological activity in the genome of an organism. For example, for the proteins of the same biological activity to be the capture agents on Wagner's arrays, or to be captured by the capture agents on Wagner's arrays, a binding partner specific to each protein, that is not cross-reactive to any of the other proteins with the same biological activity, would be needed. Taking kinases as an example, Wagner provides no guidance as to what the binding partners/capture agents would be that would recognize individually such a vast number of kinases but not be cross-reactive with any of the other kinases, such that a spatially separated array with different kinases at different patches could be generated. For example, if an antibody were to be the capture agent (or were to be the binding partner used to isolate the kinase), it is clear that to generate antibodies specific to each of more than 50% of the kinases in the genome of an organism, that would not be cross-reactive with any other kinase in the genome of the organism, would require undue experimentation, assuming *arguendo* that such antibodies could even be generated. There is clearly no teaching in Wagner of how to achieve this. The situation is similar for proteins with other types of biological activities in that Wagner does not teach how to obtain the myriad number of specific, non-crossreactive capture agents that would be required to make the arrays taught by Wagner in order to capture at least 50% of proteins (or molecules comprising functional domains thereof) with the same type of biological activity in the genome of an organism. Thus, Wagner fails to provide any teachings for how spatial separation of such a group of proteins of different identities but with the same type of biological activity could be achieved. Because Wagner is not enabling for the array of claim 1, Wagner does not anticipate claim 1.

By virtue of their dependencies, claims 2-11 and 106-107 incorporate the limitations of claim 1 and are therefore not anticipated by Wagner.

The Rejections Under 35 U.S.C. § 103 Should Be Withdrawn

Claims 93 to 101 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wagner in view of Foster et al. (U.S. Patent No. 4,444,879; "Foster"). Claims 1-13 and 15-16 are rejected as allegedly being obvious over Taylor (U.S. Patent No. 6,103,479; "Taylor"). Further, claim 14 is rejected allegedly as being obvious over Taylor in view of Wang et al. (U.S. Patent No. 5,922,617; "Wang"). For the reasons discussed below, Applicants submit that the pending claims are not obvious over the cited prior art references because the cited prior art, alone or in combination, does not teach nor suggest an array with at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, with the same type of biological activity of the genome of an organism of interest.

The Legal Standard

A finding of obviousness under § 103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Graham v. Deere 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. In re O'Farrell 853 F.2d 894, 903 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicants' disclosure. In re Vaeck 947 F.2d 488 (Fed. Cir. 1991). Further, "the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. 2142.

Claims 93-101 Are Not Obvious over Wagner and Foster

By virtue of the amended recitation of claim 1, the protein array of the kit of claim 93 is an array with at least 100 different substances per cm^2 and at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, with the same type of biological activity of the genome of an organism of interest. As set forth above, Wagner does not teach or suggest such an array.

Even though Wagner mentions at column 12, lines 23-40 that proteins that "share similarity in structure or sequence" can be bound by the protein-capture agents, Wagner fails to teach binding partners or protein-capture agents that can bind specifically to each of a

population of different proteins of a certain biological activity, but that are not cross-reactive. Moreover, Wagner fails to describe how such binding partners or protein-capture agents could be designed or obtained. At best, Wagner provides an invitation to experiment but does not provide a reasonable expectation of success of achieving the claimed invention.

Foster is cited for teaching an immunoassay kit and thus does not remedy the deficiencies of Wagner. Since claim 93 recites claim limitations that are not present in Wagner and Foster combined, these references cannot make obvious the kit of claim 93. By virtue of their dependencies from claim 93, claims 94-101 recite the limitations of claim 93 and are likewise not made obvious by Wagner in view of Foster.

Claims 1-13 and 15-16 Are Not Obvious over Taylor

Taylor describes a device for high throughput screening of cells in micro-patterned arrays. Applicants note that the present amendment to claim 1 deletes the recitation of "whole cells" as a substance on the array. Taylor also teaches that its non-uniform micro-patterned arrays may contain a variety of different cell binding molecules that permit cell attachment (column 8, lines 50-57) in order to produce the cell arrays. Taylor, however, does not teach or suggest arrays in which at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, with the same type of biological activity of the genome of an organism of interest are represented on the array. Thus, Taylor cannot make obvious any of claims 1-13 and 15-16 as amended.

Claim 14 Is Not Obvious over Taylor in View of Wang

Via its dependency from claim 12, which in turn depends from amended claim 1, claim 14 is directed to an array with at least 100 different substances per cm^2 and at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, with the same type of biological activity of the genome of an organism of interest. As discussed above, Taylor neither teaches nor suggests such an array. Wang describes a microarray of bound components but does not teach nor suggest an array with at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, with the same type of biological activity of the genome of an organism of interest. Thus, the combination of Taylor and Wang does not make obvious the invention as defined by claim 14.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date April 10, 2003

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Attachments:

Appendix A: Marked-Up Version of the Claims Showing the Changes Made herein

Appendix B: Claims Pending Upon Entry of the Present Amendment

APPENDIX A
Marked-Up Version of Claims Pending Upon Entry of the Amendment
Filed April 10, 2003
U.S. Patent Application Serial No. 09/849,781
Attorney Docket No.: 6523-028

Matter that has been deleted from claims is indicated by brackets and matter that has been added is indicated by underlining.

1. (Amended) A positionally addressable array comprising a plurality of different substances, selected from the group consisting of proteins, and molecules comprising functional domains of said proteins, [whole cells, and protein-containing cellular material,] on a solid support, with each different substance being at a different position on the solid support, wherein the plurality of different substances consists of at least 100 different substances per cm^2, wherein the plurality of proteins or molecules consists of at least 50% of all expressed proteins, or molecules comprising functional domains of said proteins, respectively, with the same type of biological activity in the genome of an organism.

93. (Amended) A kit comprising:

(a) one or more arrays of claim 1 comprising a plurality of wells on the surface of a solid support wherein the density of the wells is at least 100 wells/cm^2, wherein each of said different substances is present in a different well; and

(b) in one or more containers, one or more probes, reagents, or other second molecules.

100. (Amended) The kit according to claim 93 wherein said one or more containers contain a solution reaction mixture for assaying biological activity [of a protein or molecule].